

ISIS0003-100 (ISPH-0522)**PATENT****REMARKS**

Claims 1-4 and 19 were pending and rejected.

Claims 5-18 and 20-52 were withdrawn from consideration as directed to non-elected inventions.

The specification has been amended to remove the priority claim and also to add a sequence identifier.

Claims 1, 5-18 and 20-52 have been canceled without prejudice.

Claims 2-4 have been amended. Claim 2 was amended to clarify that the claimed human RNase III polypeptide cleaves double-stranded RNA. Claim 3 was rewritten in independent form and was amended to clarify that the claimed human RNase III polypeptide cleaves double-stranded RNA. Claim 4 was amended to specify that the claimed human RNase III polypeptide cleaves double-stranded RNA and that the polypeptide comprises an amino acid sequence which is at least 90% homologous to SEQ ID NO:2. Support for the amendments can be found throughout the application as filed, especially on pages 29-30 and 32-33, and in Examples 9 and 10 on pages 43-44.

No new matter has been added via the foregoing amendments.

Upon entry of this amendment, claims 2-4 and 19 will be pending.

Applicants thank the Examiner for the courtesies and suggestions extended to the undersigned during several teleconferences. The Examiner's suggestions have been incorporated into the present response.

Advisory Action

In an Advisory Action mailed by the Patent Office on October 10, 2003, the Office noted that the amendments filed in the Applicants' August 22, 2003 Response were not entered because, *inter alia*, "they would raise new issues" and "they are not deemed to place the application in better form for appeal." (Advisory Action). Applicants represent herein amendments to the specification. As discussed with the Examiner, claims 2-4, as amended herein, overcome the written description rejection. Although Applicants respectfully disagree that entry of a claim directed to SEQ ID NO:37 would require a new search as suggested by the Examiner, Applicants will

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prosecute claims directed at other embodiments of the present invention, including those directed to SEQ ID NO:37, in future related applications.

Priority

Applicants note the Examiner's statement that "[t]he claimed invention (claims 1-4 and 19) is awarded a priority date of, 07/06/01, the filing date of the instant application." (Final Rejection, page 2). Applicants have amended the specification to remove the original claim of priority. Applicants filed an Executed Oath/Declaration reflecting the removal of the priority claim on October 14, 2003. Accordingly, Applicants note that the earliest priority date for the present application is July 6, 2001. Applicants attach hereto a request for a corrected Filing Receipt.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 4 and 19 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. Applicants respectfully disagree because the specification sufficiently describes the claimed subject matter.

The Office indicates that:

the claims [claims 1, 2, 4 and 19] fail to provide a structure that would be correlated with a function. Claims 1, 4 and 19 provide for structures unrelated to SEQ ID NO:2 and more specifically other than that structure, the 466 C-terminal-most amino acids of SEQ ID NO:2 that provides for the function of double stranded RNA cleavage and claim 2 fails to provide for a function that would correlate with a recited structure (e.g. 90% identity but with any function that may or may not have been correlated in the art or instant specification with such a structure, for example).

(Final Rejection, page 6).

Although Applicants disagree, solely in an attempt to advance the pending claims to issuance, Applicants have amended claims 2-4 and have canceled claim 1 without prejudice. Each pending claim recites a structure with a correlated function.

Claim 2, amended herein, provides a structure, at least 90% homology to SEQ ID NO: 2, with a correlated function, cleaving double-stranded RNA.

Claim 3, amended herein, provides a structure, SEQ ID NO: 2, with a correlated function, cleaving double-stranded RNA.

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Claim 4, amended herein, provides a structure, at least 90% homology to SEQ ID NO: 2, with a correlated function, cleaving double-stranded RNA.

Applicants respectfully assert that one of skill in the art would readily acknowledge that the application as filed provides ample written description for claims 2-4 and 19.

The application as filed provides nucleotide and amino acid sequences for human RNase III (see SEQ ID NOS:1 and 2, respectively), as well as the amino acid sequence for the RNase III domain of SEQ ID NO:2 (SEQ ID NO:37). As acknowledged by the Examiner, the application also sets forth methods for identifying RNase III polypeptides which cleave double-stranded RNA (see, for example, Example 10).

Applicants respectfully assert that the genera of proteins claimed comply with the written description requirement. For example, Applicants provide representative species of the genus. There is actual reduction to practice of both SEQ ID NO:2 and SEQ ID NO:37. As discussed above, the pending claims all recite both structure and function. In the pending claims which recite a genus, there is no substantial variation between species since all of the species within the genus must have at least 90% identity to SEQ ID NO:2. Applicants provide a stated degree of homology (90%) which imposes a structural relationship between members of the genus. Applicants' specification also teaches methods for determining whether a polypeptide cleaves double-stranded RNA.

The Office Action failed to provide any evidence or reasoning why the specific species described, along with a description of the structure and function of the human RNase III that comprise the claimed genera, does not constitute adequate description of the claimed subject matter. One of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by the members of the genus and that the disclosure meets the requirements of 35 USC §112, first paragraph, as providing adequate written description for the claimed invention.

Applicants respectfully assert that the Office has misinterpreted the teaching of the Wu reference (Wu *et al.*, J. Biol. Chem., Vol. 275, No. 47, 36957-36965, 2000). The Wu reference does *not* suggest that "the species specifically disclosed [in the present application] are not representative of the genus because the genus is highly variant . . ."

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(Final Rejection, page 4). As pointed out in Applicants' "Response" to Office Action mailed April 16, 2003:

The Wu reference cites variability of known RNase III proteins *across animal species*, while the present invention discloses variability of the human RNase III polypeptide *within the human species*. The interspecies variability cited on page 36957, column 2, last paragraph of Wu (which states that "the human enzyme is distinctly different from the homologues in other species") describes RNase III interspecific homologues in other eukaryotes. Interspecific variability is not equivalent to intraspecies variability observed within the genus of human RNase III polypeptides, much less to the limited variability present in polypeptides capable of cleaving double- stranded RNA or amino acid sequences having 90% sequence homology to SEQ ID NO:2, as claimed in claims 1 and 2, respectively. While interspecies homology of the human RNase III protein of the invention is discussed in several parts of the present application (including page 6, lines 30-35, and page 7, lines 3-7, which describe a comparison of a human, RNase III amino acid sequence with RNase III amino acid sequences of other species) these other non-human species are not claimed -- Applicants claim *human* RNase III polypeptides. . . [The **maximum** variation of species within the pending claims is 90%.] . . In stark contrast, in terms of **interspecies** sequence homology, the closest RNase III to the human RNase III is in worm and shares only 41% sequence homology . . . Wu fails to support the Examiner's assertion that 'the species specifically disclosed are not representative of the genus because the genus is highly variant.'

For the foregoing reasons, Applicants respectfully request withdrawal of the written description rejection. Accordingly, reconsideration and withdrawal of this rejection is requested.

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The examination of these claims and passage to allowance are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6904 to clarify any unresolved issues raised by this response.

Respectfully submitted,


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Attachment: 1) Request for Corrected Filing Receipt

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